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Microfabricated containers for pH-triggered drug release in the upper intestine

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In the past years, microfabricated containers were introduced as new concept for oral drug delivery [1,2]. The microcontainers provide a cavity that is filled with drug formulation and sealed with a polymer membrane. In this way degradation of the drug in the stomach is prevented and the drug release is triggered by dissolution or degradation of the membrane in the intestine. Here, we present our recent advances in the development of microcontainers for oral drug delivery, with particular focus on new methods for drug loading and integration of enteric coatings.

Prototype microcontainers with inner diameters of 230 μm were fabricated using epoxy resins (SU-8, Microchem, USA) patterned by UV exposure (Fig. 1a). Alternatively, biodegradable containers were prepared. In this case hot embossing in biodegradable polymers such as Poly(lactic acid) (PLLA) was used to define the bottom and the walls of the cavities (Fig. 1b). The microcontainers were filled with drug using two different methods: a) Loading of drug powder and b) deposition of Poly(vinylpyrrolidone) (PVP) in the cavities by inkjet printing followed by supercritical drug impregnation (Fig. 2) [3]. Finally, a lid of enteric polymer (Eudragit L100, Evonik Industries, Germany) sealing the open side of the cavity was selectively deposited on the microcontainer using spray coating through a shadow mask (Fig.3) [4]. Fig.4 shows *in vitro* drug release from microcontainers loaded with ketoprofen by supercritical impregnation. Furthermore, pH-triggered release was demonstrated by *in vitro* experiments with microcontainers filled with solid dispersions of furosemide and cinnarizine and coated with Eudragit L100.

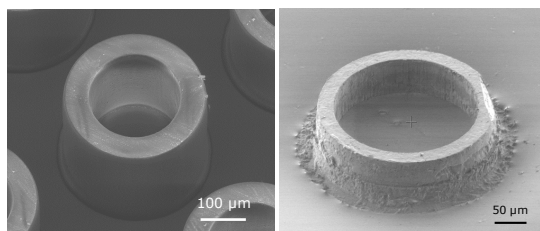


Figure 1: Microcontainers fabricated by a) UV patterning of SU-8 and b) hot embossing in PLLA

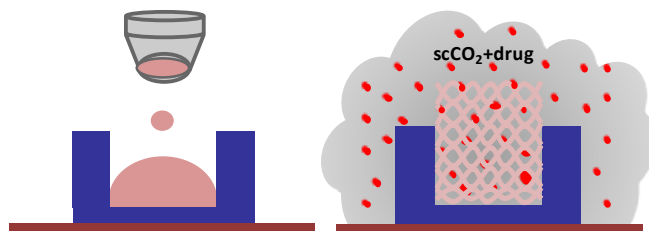


Figure 2: Drug loading combining a) inkjet printing and b) drug impregnation in supercritical CO_2

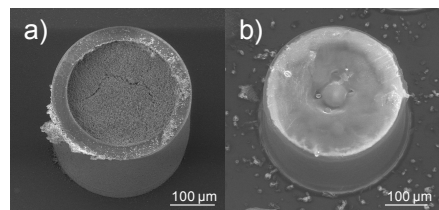


Figure 3: Microcontainers filled with drug powder a) before and b) after deposition of Eudragit L100

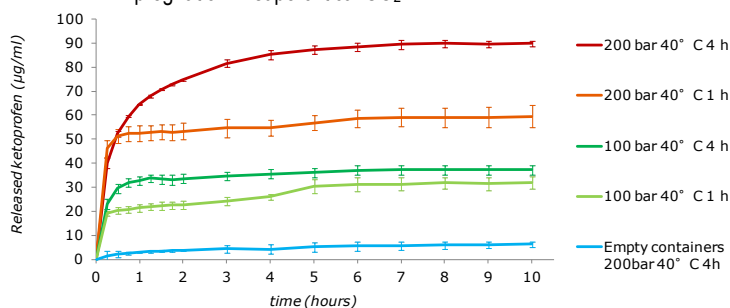


Figure 4: *In vitro* release profiles for 625 microcontainers filled with PVP and loaded with ketoprofen by supercritical impregnation

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